REMARKS

Claims 1-55 are pending in the application. No amendments have been made by the present response.

35 U.S.C. §103(a) (Obviousness)

At pages 3-6 of the Office Action, claims 1, 2, 12-14, 16-19, 23, 25, 32-40, 43-46, 54, and 55 were rejected as unpatentable over Chen et al. (1998) J. Virol. 72:5757-31 ("Chen") in view of Jones et al. (1996) Infection and Immunity 64:489-94 ("Jones") and U.S. Patent No. 6,537, 813 ("the '813 patent").

Independent claim 1 is directed to a scalable continuous process for preparing nucleic acid-containing microparticles. The method requires continuous action at the following steps (maintaining the lettering for the steps used in the claim): (b) continuously supplying a first emulsion to a mixing chamber; (c) continuously supplying a second aqueous solution to the mixing chamber; (d) continuously emulsifying the first emulsion and the second aqueous solution in the mixing chamber to form a second emulsion; and (e) continuously transferring the second emulsion from the mixing chamber to a solvent removal device. An aqueous suspension of nucleic acid-containing microparticles is ultimately formed in the solvent removal device in step (f) via diffusion of the organic solvent into an aqueous phase of the second emulsion.

Both Chen and Jones describe methods for preparing DNA encapsulated microparticles. Chen and Jones employ double emulsion preparation techniques that include the harvesting of microparticles by centrifugation. The centrifugation steps used by Chen and Jones render their processes non-continuous, as centrifugation necessarily implies the treatment of a discrete batch of product and is therefore not amenable to a continuous process. As a result, Chen and Jones do not describe or suggest a "scalable continuous process" for the preparation of microparticles, as is required by claim 1.

The Office Action acknowledged (at page 4) that "Chen et al. and Jones et al. do not teach a scalable continuous process (claim 1) ..." However, the Office Action asserted (at page 5) that

> [i]t would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Chen et al. and Jones et al. by using the apparatus of Chen et al. ('813), with a reasonable expectation of success. The motivation to do so is provided by Chen et al. (813), who teach that no other mixing format allows for convenient, reliable, reproducible, and sclaleable process that results in the production of uniform quality and particle size specific for different applications (column 6, bridging column 7, column 10 bridging column 11).

Applicants respectfully contest the assertion that the person of ordinary skill in the art having read Chen, Jones, and the '813 patent would have had any basis to modify the centrifugation-based (non-continuous) batch method of Chen and Jones to derive a scalable continuous process for preparing nucleic acid-containing microparticles.

The '813 patent describes methodologies and apparatuses for concurrent flow mixing (referred to as "CFM") of gene therapy vectors and associated vehicles. The CFM techniques of the '813 patent entail providing a first molecular entity-containing solution, a second molecular entity-containing solution, and a flow through mixer and simultaneously introducing the first and second solutions into the mixer. The '813 patent discloses that its CFM methods may be carried out as a continuous process. In the practice of a continuous CFM process, each reagent is continuously fed into a dispenser connected to the mixer whereby it is unnecessary to halt operation of the process to load new reagents into the system (the '813 patent at column 21, lines 47-57).

As noted in the passage from the Office Action reproduced above, the '813 patent places significant emphasis on the advantages of CFM as compared to other mixing technologies. For example, the '813 patent states the following:

- "[N]o other mixing format [other than CFM] allows for convenient, reliable, reproducible, and scaleable methodologies." (the '813 patent at column 10, lines 56-58; emphasis added)
- "These characteristics of CFM, as adapted to gene therapy vector and vehicle compositions, are essential for obtaining reliable clinical data with respect to

safety and efficacy, and ultimately commercialization." (the '813 patent at column 10, lines 58-61; emphasis added)

- "[W]hen a condensed nucleic acid composition is desired, no other mixing format [other than CFM] allows for reproducible and strict control over particle size." (the '813 patent at column 10, lines 61-64; emphasis added)

The statements above from the '813 patent convey in unambiguous terms that mixing formats other than CFM do not allow for scalable methodologies having the advantages associated with the CFM technique. In view of this teaching, the person of ordinary skill in the art would not have considered the '813 patent as having provided the rationale to use a technique other than CFM by attempting to modify the double emulsion methods of Chen and Jones so as to render them continuous. Instead, the '813 patent would have conveyed to the skilled person the importance of using the CFM technology (in either a continuous or non-continuous format) for preparing compositions containing a gene therapy vector and a vehicle.

In addition to the failure of the '813 patent to provide the person of ordinary skill in the art with any rationale to seek to modify the methods of Chen and Jones so as to render those methods continuous, the '813 patent contains no teaching as to how such a modification might be achieved. As described above, the double emulsion techniques of Chen and Jones employ a centrifugation step for the harvesting of microparticles. This centrifugation step necessarily renders the batch methods of Chen and Jones non-continuous. The '813 patent contains no detailed teaching regarding the preparation of nucleic acid-containing microparticles and provides no instruction as to how the impediment to a continuous process presented by a centrifugation step might be overcome. Of particular relevance to the present obviousness rejection, the '813 patent contains no instruction as to how to harvest microparticles in the absence of a centrifugation step so as to permit the performance of a continuous double emulsion technique. The '813 patent's CFM technique differs from the double emulsion techniques of Chen and Jones and provides no suggestion as to how a double emulsion technique could be modified to render it continuous. As a result, the person of ordinary skill in the art having read Chen, Jones, and the '813 patent would have been left not only with no rationale for attempting

to modify the double emulsion methods of Chen and Jones to make them continuous but with no instruction as to how such a modification might be achieved.

In view of the forgoing remarks, applicants respectfully submit that the combination of Chen, Jones, and the '813 patent does not render obvious the claimed methods. Applicants request that the Examiner withdraw the rejection of independent claim 1 and claims 2, 12-14, 16-19, 23, 25, 32-40, 43-46, 54, and 55 that depend therefrom.

At pages 7-8 of the Office Action, claims 1-6, 12-19, 23, 25, 32-46, 48-50, 54, and 55 were rejected as unpatentable over Chen taken with Jones and the '813 patent in further view of Shah, U.S. Patent No. 6,020,004 and Parikh et al., U.S. Patent No. 5,660,858 ("Parikh").

The Office Action cited Shah and Parikh as allegedly describing features of various dependent claims and asserted that it would have been obvious to modify the methods of Chen taken with Jones and the '813 patent in view of Shah and Parikh to arrive at the methods of these dependent claims.

As detailed above, the combination of Chen, Jones, and the '813 patent does not render obvious the method of independent claim 1. Shah and Parikh provide nothing that supplements the deficiencies of Chen, Jones, and the '813 patent or renders obvious the method of independent claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

At pages 8-9 of the Office Action, claims 1, 2, 10-14, 16-19, 23, 25-28, 32-40, 43-47, 54, and 55 were rejected as unpatentable over Chen taken with Jones and the '813 patent in further view of U.S. Published Application Number 20020039596 ("Hartounian") and Shah.

The Office Action cited Hartounian and Shah as allegedly describing features of various dependent claims and asserted that it would have been obvious to modify the methods of Chen taken with Jones and the '813 patent in view of Hartounian and Shah to arrive at the methods of these dependent claims.

As detailed above, the combination of Chen, Jones, and the '813 patent does not render obvious the method of independent claim 1. Hartounian and Shah provide nothing that supplements the deficiencies of Chen, Jones, and the '813 patent or renders obvious the method of independent claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

At pages 9-10 of the Office Action, claims 1, 2, 12-14, 16-19, 23, 25, 29-40, 43-46, and 51-55 were rejected as unpatentable over Chen taken with Jones and the '813 patent in further view of Hedley et al., U.S. Patent No. 5,783,567 ("Hedley").

The Office Action cited Hedley as allegedly describing features of various dependent claims and asserted that it would have been obvious to modify the methods of Chen taken with Jones and the '813 patent in view of Hedley to arrive at the methods of these dependent claims.

As detailed above, the combination of Chen, Jones, and the '813 patent does not render obvious the method of independent claim 1. Hedley provides nothing that supplements the deficiencies of Chen, Jones, and the '813 patent or renders obvious the method of independent claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

At page 10 of the Office Action, claims 1, 2, 12-14, 16-19, 20-25, 32-40, 43-46, 54, and 55 were rejected as unpatentable over Chen taken with Jones and the '813 patent in further view of Tice et al., U.S. Patent No. 4,389,330 ("Tice").

The Office Action cited Tice as allegedly describing features of various dependent claims and asserted that it would have been obvious to modify the methods of Chen taken with Jones and the '813 patent in view of Tice to arrive at the methods of these dependent claims.

As detailed above, the combination of Chen, Jones, and the '813 patent does not render obvious the method of independent claim 1. Tice provides nothing that supplements the deficiencies of Chen, Jones, and the '813 patent or renders obvious the method of independent

claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance.

Enclosed is a Petition for Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 08191-012002.

Respectfully submitted,

Date: October 15, 2010

/Jack Brennan/
Jack Brennan
Reg. No. 47,443

Customer Number 26161
Fish & Richardson P.C.
Telephone: (212) 765-5070
Facsimile: (877) 769-7945